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EXAMINER	
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1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/001,245	HOLM ET AL.	
	Examiner	Art Unit	
	NORA M. ROONEY	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22,35,37-39,64 and 66-85* is/are pending in the application.

4a) Of the above claim(s) *16 and 18-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15, 17, 35, 37-39, 64 and 66-85* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/31/2007 has been entered.

2. Applicant's election without traverse of the species of Der p 2 allergen with the mutation K15E S24N H30G K48A E62S K77N K82N K100N of SEQ ID NO:36 in the reply filed on 07/09/2008 is acknowledged.

3. Claims 16 and 18-22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 07/09/2008. It is noted that Applicant believes that the elected species reads on claims 1-6, 8-14, 17, 35, 64, 66-72 and 79-80. At this time the Examiner extended the examination of claims to include additional claims.

4. Claims 1-15, 17, 35, 37-39, 64 and 66-85 are currently pending and under consideration as they read on the recombinant mutant Der p 2 allergen of SEQ ID NO:36.

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 1-22, 25, 26, 28, 35, 37-39, 64, and 66-85 stand provisionally rejected under the judicially created .doctrine of obviousness-type double patenting as being unpatentable over claims 36-96 of copending Application No. 10/719,553. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims arrive at similar allergenic variants, and by what appears to the Examiner by the same method of selection, or if not by an obvious variant thereof. Specifically, Claims 36-96 teach a mutant Bet V 1 allergen with 1 or more substitutions, wherein said substitutions occur at many amino acid residues that are identical between the '553 application and the instant application, such as those recited in copending claim 37 and instant claim 22.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant has acknowledged this provisional rejection in the reply filed on 10/31/2007 and has asked that it be held in abeyance at this time.

The rejection is maintained.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claim 67 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "by at least 30 A" in claim 67 is indefinite because it depends on claim 2 which recites that the mutations be "spaced from each other by between about 20 to 30 A." Claim 67 does not narrow the scope of claim 2.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-15, 17, 35, 37-39, 64 and 66-85 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons as set forth in the Office Action mailed on 03/09/2007.

Applicant's arguments filed on 10/31/2007 have been fully considered, but are not found persuasive.

Applicant argues:

> "In response, without conceding the validity of the rejection or the Examiner's position, the claims have been amended to be directed to recombinant mutant allergens of a naturally occurring allergen selected from the group consisting of Fagales group 1 allergens, Vespidae antigen 5 allergens, house dust mite group 1 allergens, house dust mite group 2 allergens and grass group 5 allergens. *See* claim 1. The subsisting claims are thus directed to recombinant mutant allergens derived from Fagales group 1 allergens, Vespidae antigen 5 allergens, house dust mite group 1 allergens, house dust mite group 2 allergens and grass group 5 allergens and comprising at least four mutations, which each reduce the specific IgE binding capability of the mutated allergen as compared to the IgE binding capability of the naturally occurring allergen, each of said at least four mutations being a substitution of one surface-exposed amino acid residue with another residue, which does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic species from which said naturally occurring allergen originates, each of said at least four mutations being spaced from each other by at least 15 A, and comprising at least one circular surface region with a area of 800 A2 that comprises no mutation.
>
> The specification provides adequate written description for the claimed recombinant mutant allergens. The written description requirement requires that the specification provide disclosure that allows one of ordinary skill in the art of the invention to "recognize that [the inventor] invented what is claimed." *Lockwood v. American Airlines, Inc.,* 107 F.3d 1565, 1572 (Fed. Cir. 1997); *see also Vas-Cath Inc. v. Mahurkar,* 935 F.2d 1555, 1563-64 (Fed. Cir. 1991) (Applicant "must convey with reasonable clarity to those skilled in the art that ... he or she was in possession *of the invention.")* (emphasis in original). The written description requirement"ensure[s] that the scope of the fight to exclude, as set forth in the claims, does not overreach the scope of the inventor's contribution to the field of art as detailed in the patent specification." *Reiffin v. Microsoft Corp.,* 214 F.3d 1342, 1354 (Fed. Cir. 2000). The written description requirement is met by providing sufficient structural, physical and/or functional properties that describe a genus and/or a sufficient members of genus that show the inventors were in possession of the claimed invention. *Regents of the University of California v. Eli Lilly & Co.,* 119 F.3d 1559, 1567-68 (Fed. Cir. 1997). Functional language may provide adequate written description "if in the knowledge of the art the

disclosed function is sufficiently correlated with a particular, known structure." *Amgen Inc. v. Hoechst Marion Roussel, Inc.,* 314 F.3d 1313, 1332 (Fed. Cir. 2003) *citing Enzo Biochem, Inc. v. Gen-Probe, Inc.,* 296 F.3d 1316, 1324 (Fed. Cir. 2002).

The instant application sets forth the claimed invention in sufficient detail to show that Applicants were in possession of the claimed invention. Hence, the specification discloses that "the invention is based on the recognition that a mutated allergen having IgE binding reducing mutations in multiple be cell epitopes, and at least one intact epitope" would reduce crosslinking IgE, and thus the allergenicity of the mutant allergens, while preserving at least one epitope to raise an IgG response. Specification at page 18, lines 29-36. The specification discloses that the recombinant mutant allergens are produced by making substitutions of at least four surfaced- exposed, conserved amino acids that are spaced from each other by at least 15 ~, while preserving at least one circular surface region of 800 ~2. Specification at, e.g., page 19, line 21-page 20, line 1. The spacing of the at least four mutations ensures that they are in separate clusters of epitopes. Specification at page 20, lines 14-17. In addition to the at least four mutations spaced at least 15 from each other, the recombinant mutant allergens may further comprise additional mutations ("secondary mutations") that further reduce IgE binding. Specification at page 24, line 27 through page 25, line 8. These additional mutations are also placed such that a 800/~2 area free of mutations is preserved. Specification at page 25, lines 2-3. The specification further sets forth detailed "Criteria for substitution." Specification at page 36-38.

The specification further gives detailed analysis on the structural features of Bet v 1, Der p 2, Ves v 5, Der p 1, and Phl p 5 and related proteins that further show possession of the claimed invention. Thus, the specification discloses 57 amino acids of Bet v 1 that are highly solvent exposed and conserved (page 68), 54 amino acids of Der p 2 that are highly solvent exposed and conserved (page 72), 88 amino acids of Ves v 5 that are highly solvent exposed and conserved (page 76) and sets forth 12 Der p 2 mutants (pages 97-98), 11 Der p 1 mutants (pages 105-106), 14 Phl p 5 mutants (pages 114-115). The detailed description of amino acids to be mutated and the combinations of mutants demonstrate that the inventors had possession of the claimed invention as it relates to Bet v 1, Ves v 5, Derp 1, Derp 2, andPhl p 5. Moreover, as disclosed in the specification, Bet v 1, Ves v 5, Der p 1, Der p 2, and Phl p 5 are highly homologous to allergens Fagales group 1 allergens, Vespidae antigen 5 allergens, house dust mite group 1 allergens, house dust mite group 2 allergens and grass group 5 allergens, respectively. See specification at page 81, lines 1-15 (67 sequences homologous to Bet v 1 within the order Fagales), page 58 and Fig. 10 A (Vespula Ag 5s about 90% identical), Fig. 35 A and B (sequence alignment of Der p 1 and other house dust mite group 1 allergens), Fig. 32 (sequence of Der p 2 with other house dust mite group 2 allergens), and Fig. 38 A-D (sequence alignment of Phl p 5 with other grass group 5 allergens). One of ordinary skill in the art would understand that the high degree of sequence identity among the members of the respective allergen families recited in the claims means that description of recombinant mutant allergens for a single member of the family provides written description for recombinant mutant allergens of any allergen within the same family. Thus, the specification provides written description for the recombinant mutant allergens called for in the subsisting claims.

In setting forth the instant rejection, the Examiner cites *Eli Lilly, supra.* The nature of the instant invention and the disclosure of the instant specification, however, are very different from *Eli Lilly. In Eli Lilly,* the Federal Circuit held that the disclosure of the sequence of a rat insulin cDNA did not provide adequate written description for the insulin cDNA sequence of every vertebrate. *Eli Lilly* at 1566-67. In *Eli Lilly,* however, the specification failed to provide any features that described the claimed vertebrate insulin cDNA. The Court found that the claimed cDNA were described solely by their function or how to obtain them. The instant case is inapposite to *Eli Lilly. In Eli Lilly* the claims were directed to unknown cDNA sequences. The instant claims, by contrast, are drawn to mutant allergens that are derived by making substitutions in a family of allergens, i.e., Fagales group 1 allergens, Vespidae antigen 5 allergens, house dust mite group 1 allergens, house dust mite group 2 allergens and grass group 5 allergens, with closely related sequences. In *Eli Lilly,* no structural features were provided that correlated with the function of the claimed vertebrate insulin cDNA. In the instant case, the specification provides that substituted amino acids

are those amino acids that are conserved, solvent accessible amino acids that are spaced at least 15 A from each other and which are each outside a circular area of 800 A2 on the surface of the allergen and goes on to list particular amino acids to choose among to make the claimed recombinant mutant allergens.

Nor does the decision of the Board of Patent Appeals and Interferences in *ex parte Kubin* (83 U.S.P.Q.2d 1410 (BPAI 2007)) support a finding that the instant specification fails to provide adequate written description for the pending claims. In *Kubin,* the Board upheld the rejection of a claim directed to isolated polynucleotides encoding polypeptides that (1) "are at least 80% identical to amino acids 22-221 of SEQ ID NO: 2" (i.e., the amino acid sequence for the extracellular domain of the protein natural killer cell activation inducing ligand ("NAIL") lacking the NAIL signal sequence) and (2) which bind to the glycoprotein CD 48. *Id.* at 1417. The specification in *Kubin* disclosed the sequence of two nucleic acids within the scope of the claim and three fusion proteins whose nucleic acid sequences would fall within the scope of the claim. *Id.* None of these sequences varied amino acids 22-221 of SEQ ID NO: 2. *Id.*

The Board in *Kubin* found that the Applicant had failed to describe what domains of within amino acids 22-221 of SEQ ID NO: 2 correlated with the function of binding CD 48, and thus the Applicant had not described which NAIL amino acids could be varied and still maintain CD 48 binding. *Id.* Citing *Eli Lilly,* the Board found that in the absence of a structure-function correlation, the claim merely defined the invention by function, which was not sufficient to satisfy the written description requirement.

Kubin is distinguished from the instant case for much the same reasons as *Eli Lilly.* In *Kubin,* the Applicant failed to provide any features of amino acids 22-221 of SEQ ID NO: 2 that correlated with binding to CD 48. As set forth above, the instant specification, in contrast, allows one of ordinary skill in the art to identify amino acids Fagales group 1 allergens, Vespidae antigen 5 allergens, house dust mite group 1 allergens, house dust mite group 2 allergens and grass group 5 allergens. Furthermore, whereas in *Kubin* the Applicant failed to disclose any polynucleotides encoding NAIL protein that varied in amino acids 22-221, the instant applications identifies numerous amino acid for substitution in Fagales group 1 allergens, Vespidae antigen 5 allergens, house dust mite group 1 allergens, house dust mite group 2 allergens and grass group 5 allergens, and further sets forth examples of combinations of mutants, whereas the Applicant in *Kubin* failed to provide any working examples of polynucleotides encoding a polypeptide at least 80% identical to amino acids 22-221 of SEQ ID NO: 2 and which bind CD 48.

In short, as with *Eli Lilly,* the Applicant in *Kubin* failed to provide any structural features that correlated with the function of the polypeptide called for in the claim, whereas the instant specification sets out the features, including specific amino acids, of Fagales group 1 allergens, Vespidae antigen 5 allergens, house dust mite group 1 allergens, house dust mite group 2 allergens and grass group 5 allergens that are called for in the claims and which allow one of ordinary skill in the mutant art to make the claimed recombinant allergens. Thus, the basis of the Board's decision in *Kubin* does not apply to the instant claims. "

It remains the Examiner's position that the specification does not disclose a correlation between the structure of the claimed recombinant allergens (complete combinations of specific mutations to a reference sequence) and function (which each reduce the specific IgE binding capability of the mutated allergen as compared to the IgE binding capability of said naturally occurring allergen) and in this case functional limitations (see below bolded portions) such that a

skilled artisan would have known what modifications to make to the allergens to attain the claimed function and functional limitations. "Possession may not be shown by merely describing how to obtain possession of member of the claimed genus or how to identify their common structural features" *Ex parte Kubin* (83 U.S.P.Q.2d 1410 (BPAI 2007)), at page 16. In this instant case Applicants have not provided any guidance as to what mutation or combination of mutations will result in the claimed functions and functional limitations. "Without a correlation between structure and function, the claim does little more than define the claimed invention by function" *supra*, at page 17.

A recombinant mutant allergen of a naturally occurring allergen, said naturally occurring allergen selected from the group consisting of Fagales group 1 allergens, Vespidae antigen 5 allergen$_s$, house dust mite group 1 allergens, house dust mite group 2 allergens and grass group 5 allergens and comprising wherein at least four mutations, which each reduce the specific IgE binding capability of the mutated allergen as compared to the IgE binding capability of said naturally occurring allergen, **each of said at least four mutations being is a substitution of one surface-exposed amino acid residue with another residue, which does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic species from which said naturally occurring allergen originates, each of said at least four mutations being is spaced from each other by at least 15 A, and said mutant allergen comprising at least one circular surface region with a area of 800 A that comprises no mutation** of claim 1;

wherein the **each of said at least four mutations is spaced from each other by between**
about 20 to 30 A of claim 2;

wherein said **at least four mutations are spaced from each other by at least 25 A** of claim 66;

wherein said **at least four the primary mutations are spaced from each other by at least 30 A** of claim 67;

which comprises at least five mutations in total, which each reduces the specific IgE binding capability of the mutated allergen as compared to the IgE binding capability of

said naturally occurring allergen, **each of said at least five mutations in total being a substitution of one surface- exposed amino acid residue with another residue, which does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic species from which said naturally occurring allergen originates, and at least two of said at least five mutations in total being spaced within 15 A of each other** of claim 3;

which comprises at least 8 total mutations and **wherein each of said at least four mutations spaced from each other by at least 15 A is spaced within 15 A of 1 to 4 of said at least 8 total mutations** of claim 15;

wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen has a solvent accessibility of above 20 % of claim 4;

wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen has a solvent accessibility of above 30 % of claim 68;

wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen has a solvent accessibility of above 40 % of claim 69;

wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen has a solvent accessibility of above 50 % of claim 70

wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen is conserved with more than 70 % identity in all known homologous proteins within the species from which said naturally occurring allergen originates of claim 5;

wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen is conserved with more than 80 % identity in all known homologous proteins within the species from which said naturally occurring allergen originates of claim 71;

wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen is conserved with more than 90 % identity in all known homologous proteins within the species from which said naturally occurring allergen originates of claim 72

which essentially has the same (x-carbon backbone tertiary structure as said naturally occurring allergen of claim 6;

characterized in that when comparing the. (x-carbon backbone tertiary structures of the mutant and the naturally occurring allergen molecules, the average root mean square deviation of the atomic coordinates is below 2A of claim 9;

wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic genus from which said naturally occurring allergen originates of claim 7;

wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic subfamily from which said naturally occurring allergen originates of claim 73;

wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic family from which said naturally occurring allergen originates of claim 74;

wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic superfamily from which said naturally occurring allergen originates of claim 75;

wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic legion from which said naturally occurring allergen originates of claim 76;

wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic suborder from which said naturally occurring allergen originates of claim 77;

wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic order from which said naturally occurring allergen originates of claim 78;

characterized in that the specific IgE binding to the mutated allergen is reduced by at least 5% of claim 8;

characterized in that the specific IgE binding to the mutated allergen is reduced by at least 10% of claim 79;

characterized in said circular surface region comprises atoms of 15-25 amino acid residues of claim 10;

characterized in that the surface-exposed amino acid residues are ranked with respect to solvent accessibility, and that one or more amino acids among the more solvent accessible ones are substituted of claim 11;

characterized in that the surface-exposed amino acid residues are ranked with respect to degree of conservation in all known homologous proteins within the species from which said naturally occurring allergen originates, and that one or more amino acids among the more conserved ones are substituted of claim 12;

wherein the mutant allergen is a non-naturally occurring allergen of claim 13;

comprising from 5 to 20 mutations that reduce the specific IgE binding capability of the mutated allergen as compared to the IgE binding capability of said naturally occurring allergen, **each of said 5 to 20 mutations being a substitution of one surface-exposed amino acid residue with another residue, which does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic species from which said naturally occurring allergen originates, and each of said 5 to 20 mutations being spaced from each other by at least 15 A** of claim 14;

comprising from 6 to 15 mutations that reduce the specific IgE binding capability of the mutated allergen as compared to the IgE binding capability of the said naturally occurring allergen, **each of said 6 to 15 mutations being a substitution of one surface-exposed amino acid residue with another residue, which does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic species from which said naturally occurring allergen originates, and each of said 6 to 15 mutations being spaced from each other by at least 15 A** of claim 80;

comprising from 7 to 12 mutations that reduce the specific IgE binding capability of the mutated allergen as compared to the IgE binding capability of the said naturally occurring allergen, **each of said 7 to 12 mutations being a substitution of one surface-exposed amino acid residue with another residue, which does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic species from which said naturally occurring allergen originates, and each of said 7 to 12 mutations being spaced from each other by at least 15 A** of claim 81;

comprising from 8 to 10 primary mutations that reduce the specific IgE binding capability of the mutated allergen as compared to the IgE binding capability of the said naturally occurring allergen, **each of said at said 8 to 10 mutations being a substitution of one surface-exposed amino acid residue with another residue, which does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic species from which said naturally occurring allergen originates, and each of said 8 to 10 mutations being spaced from each other by at least 15A** of claim 82;

wherein said naturally occurring allergen is a house dust mite group 2 allergen selected from the group consisting of Der p 2, Der f 2 and Lep d 2 of claim 17;

a pharmaceutical composition comprising the recombinant mutant allergen according to claim 1 and at least one of a pharmaceutically acceptable carrier, excipient, or adjuvant of claim 35;

a composition comprising two or more recombinant mutant allergens **wherein each of said two or more recombinant mutant allergens respectively comprises at least one mutation among said at least four mutations spaced at least 15 A from each other**

that is absent in at least one other of said two or more recombinant mutant allergens of claim 37;

further comprising at least one of a pharmaceutically acceptable carrier, excipient, or adjuvant of claim 39

a composition according to claim 37 comprising 2-12 recombinant mutant allergens of claim 38;

comprising 3-10 recombinant mutant allergens of claim 83; comprising 4-8 recombinant mutant allergens of claim 84;

comprising 5-7 recombinant mutant allergens of claim 85; and

comprising at least one T cell epitope capable of stimulating a T cell clone or T cell line specific for the naturally occurring allergen of claim 64.

It is also the Examiner's position that the specification also has also not adequately described the genus of compositions "comprising two or more recombinant mutant allergens" of claim 37: comprising 2-12 recombinant mutant allergens" of claim 38; "comprising 3-10 recombinant mutant allergens" of claim 84; or "comprising 5-7 recombinant mutant allergens" of claim 85 for use in the claimed invention. Claims 35 and 39 recite compositions comprising pharmaceutically acceptable carrier, excipient or adjuvant, but the specification has not adequately described the genus of mutant allergens that can be used in a pharmaceutical composition.

Applicant has disclosed only the specific recombinant mutants of Ves v 5, Bet v 1, Der p 2, Der p 1 and Phl p 5 in Examples 1-10 in the specification; therefore, the skilled artisan cannot envision all the contemplated recombinant allergen mutant possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the

structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on (571) 272-0878. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

September 29, 2008
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